Client: Example Client ABC123
123 Test Drive
Salt Lake City, UT 84108
UNITED STATES

Physician: Doctor, Example

Patient: Patient, Example

DOB	Unknown
Gender:	Unknown
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	00/00/0000 00:00

Charcot-Marie-Tooth (CMT) and Related Hereditary Neuropathies, PMP22 Deletion/Duplication with Reflex to Sequencing Panel

ARUP test code 2012155

Charcot-Marie-Tooth Reflex Specimen: Whole Blood

Charcot-Marie-Tooth (CMT) Reflex Interp: Negative

RESULT
No pathogenic variants were detected in any of the genes tested.

INTERPRETATION
No pathogenic variants were detected by deletion/duplication analysis of the PMP22 gene; therefore, massively parallel sequencing of genes associated with Charcot-Marie-Tooth (CMT) disease and other hereditary neuropathies was performed. No pathogenic variants were identified by massively parallel sequencing of the coding regions and exon-intron boundaries of the genes tested. This result decreases the likelihood of, but does not exclude, a diagnosis of CMT or other hereditary neuropathy. Please refer to the background information included in this report for a list of the genes analyzed and limitations of this test.

RECOMMENDATIONS
Medical screening and management should rely on clinical findings and family history. Genetic consultation is recommended.

COMMENTS
Likely benign and benign variants are not reported.
Variants in the following region(s) may not be detected by NGS with sufficient confidence in this sample due to technical limitations; reportable variants are confirmed by Sanger sequencing:
NONE

This result has been reviewed and approved by [redacted]

BACKGROUND INFORMATION: Charcot-Marie-Tooth (CMT) and Related Hereditary Neuropathies, PMP22 Deletion/Duplication with Reflex to Sequencing Panel

CHARACTERISTICS: Charcot-Marie-Tooth (CMT), hereditary sensory neuropathies (HSN), hereditary sensory and autonomic neuropathy (HSAN), distal hereditary motor neuropathies (dHMN), and hereditary neuropathy with liability to pressure palsies (HNPP).

EPIDEMIOLOGY: Incidence of hereditary neuropathy is approximately 1/3,000; CMT is 1/5,000.

H=High, L=Low, *=Abnormal, C=Critical

INHERITANCE: Gene-dependent; autosomal dominant, autosomal recessive, or X-linked.

CLINICAL SENSITIVITY: greater than 70-80 percent for CMT1; 20-30 percent for CMT2; greater than 25 percent for CMT4; greater than 90 percent for CMTX; 15-20 percent for HMN; approximately 30 percent for HSN; approximately 99 percent for HNPP.

GENES TESTED:
Deletion/duplication Analysis: PMP22
Sequencing Panel: AARS, AIFM1, ATL1, ATP7A, BAG3, BICD2, BSCL2, CCT5, DCTN1, DHTKD1, DNAJB2, DNM2, DNMT1*, DYNC1H1, EGR2, ELP1, FBLN5, FGD4, FIG4, GAN, GARS, GDAP1, GJB1, GNB4, HARS, HEXA, HINT1, HOXD10, HSPB1, HSPB3, HSPB8, IGHMBP2, INF2, KARS, KIF1A, KIF1B, KIF5A, LAS1L, LITAF, LMNA, LRSAM1, MARS, MED25, MFN2, MORC2, MPZ, MTMR2, NDRG1, NEFL, NGF, NTRK1, PDK3, PLEKHG5, PMP22, PRNP, PRPS1, PRX, RAB7A, REEP1, RETREG1, SBF1, SBF2, SCN9A, SETX*, SH3TC2, SLC12A6, SLC5A7, SPTLC1*, SPTLC2, TDP1, TFG, TRIM2, TRPV4, TTR, WNK1, YARS

* - One or more exons are not covered by sequencing for the indicated gene; see limitations section below.

METHODOLOGY: Multiplex ligation-dependent probe amplification (MLPA) of the PMP22 gene. If results were negative or inconclusive, testing reflexed to targeted capture of all coding regions and intron-exon boundaries of the genes listed above followed by massively parallel sequencing. Sanger sequencing was performed as necessary to fill in regions of low coverage and confirm reported variants Human genome build 19 (Hg 19) was used for data analysis.

ANALYTICAL SENSITIVITY: 99 percent for MLPA. The analytical sensitivity of this for sequencing is approximately 99 percent for single nucleotide variants (SNVs) and greater than 93 percent for insertions/duplications/deletions from 1-10 base pairs in size. Variants greater than 10 base pairs may be detected, but the analytical sensitivity may be reduced.

LIMITATIONS: A negative result does not exclude a heritable form of neuropathy. This test only detects variants within the coding regions and intron-exon boundaries of the targeted genes. Regulatory region variants and deep intronic variants will not be identified and breakpoints of large deletions/duplications will not be determined. Deletions/duplications/insertions of any size may not be detected by massive parallel sequencing. Diagnostic errors can occur due to rare sequence variations. In some cases, variants may not be identified due to technical limitations in the presence of pseudogenes, repetitive, or homologous regions. This assay may not detect low-level somatic variants associated with disease. Interpretation of this test result may be impacted if this patient has had an allogeneic stem cell transplantation. Non-coding transcripts were not analyzed.

The following regions are not sequenced due to technical limitations of the assay:
SPTLC1(NM_006415) exon(s) 3
DNMT1(NM_001130823) exon(s) 5
SETX(NM_001351528) exon(s) 26

This test was developed and its performance characteristics determined by ARUP Laboratories. It has not been cleared or approved by the US Food and Drug Administration. This test was performed in a CLIA certified laboratory and is intended for clinical purposes.

Counseling and informed consent are recommended for genetic testing. Consent forms are available online.

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
Charcot-Marie-Tooth Reflex Specimen	22-209-102196	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Charcot-Marie-Tooth (CMT) Reflex Interp	22-209-102196	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00

END OF CHART

H=High, L=Low, *=Abnormal, C=Critical